thus are fully supported by the specification and do not present any new matter. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter. Claims 43-73, 223-229, 263-268, and 316-317 are therefore pending with entry of this amendment.

43. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:1-21 and 95-142, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b); and

(d) a polynucleotide sequence comprising all or a nucleotide fragment of (a), (b), or (c), wherein the nucleotide fragment encodes a polypeptide having a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or a polypeptide having an ability to induce a T cell proliferation response that is about equal to or greater than that induced by human B7-1.

44. An isolated or recombinant nucleic acid comprising a polynucleotide sequence encoding a polypeptide, wherein the encoded polypeptide comprises an amino acid sequence which is substantially identical over at least about 150 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293 and is a non naturally-occurring amino acid sequence.

45. The nucleic acid of claim 44, wherein the encoded polypeptide is substantially identical over at least about 175 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

46. An isolated or recombinant nucleic acid comprising a nucleotide sequence coding for a polypeptide comprising the amino acid sequence set forth in any of SEQ ID NOS:48-

68, 174-221, 283-285, and 290-293, or a subsequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide, the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide, and wherein the amino acid sequence or subsequence is a non naturally-occurring sequence.

47. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or an ability to induce a T cell proliferation response equal to or greater than that of human B7-1.

48. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

49. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide has a decreased or a lowered binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

50. The nucleic acid of claim 43, 44, 46, or 49, wherein the encoded polypeptide induces T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

51. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

52. The nucleic acid of claim 43, 44, or 46, wherein the nucleic acid encodes a fusion protein comprising at least one additional amino acid sequence.

53. The nucleic acid of claim 52, wherein the at least one additional amino acid sequence comprises at least one Ig polypeptide.

54. The nucleic acid of claim 53, wherein the at least one Ig polypeptide comprises at least one human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

55. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises a signal sequence.

56. The nucleic acid of claim 43, 44, 46, or 49, wherein the encoded polypeptide comprises a precursor peptide.

57. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises an epitope tag sequence.

58. A cell comprising the nucleic acid of claim 43, 44, 46, or 49.

59. The cell of claim 58, wherein the cell expresses a polypeptide encoded by the nucleic acid.

60. A vector comprising the nucleic acid of claim 43, 44, 46, or 49.

61. The vector of claim 60, wherein the vector comprises a plasmid, a cosmid, a phage, a virus, a virus-like particle, or a fragment of a virus.

62. The vector of claim 60, wherein the vector is an expression vector.

63. The expression vector of claim 62, wherein the nucleic acid is operably linked to a promoter.

64. The expression vector of claim 62, further comprising a polynucleotide sequence encoding an antigen.

65. The expression vector of claim 64, wherein the antigen is a cancer antigen.

66. The expression vector of claim 64, wherein the nucleic acid is operably linked to first promoter and the polynucleotide sequence encoding the antigen is operably linked to a second promoter.

67. The expression vector of claim 65, wherein the cancer antigen is EpCam/KSA or a mutant or variant thereof.

68. The expression vector of claim 67, wherein the expression vector comprises the vector shown in Figure 22B.

69. A host cell comprising the vector of claim 60.

70. A composition comprising the nucleic acid of claim 43, 44, 46, or 49 and an excipient.

71. The composition of claim 70, wherein the excipient is a pharmaceutically acceptable excipient.

72. A composition of matter comprising at least one nucleic acid of claim 43, 44, 46, or 49.

73. The composition of claim 72, wherein the composition comprises a library comprising at least about 2, 5, 10, 50 or more nucleic acids.

223. A method of modulating an immune response in a subject, comprising: administering to the subject a polynucleotide comprising a nucleic acid sequence of claim 43, 46, 128, 129, 132, or 170, operably linked to a promoter sequence that controls the expression of said nucleic acid sequence, said polynucleotide being present in an amount sufficient that uptake of said polynucleotide into one or more cells of the subject occurs and sufficient expression of said nucleic

acid sequence results to produce an amount of a polypeptide effective to modulate an immune response.

224. The method of claim 223, further comprising administering to the subject an antigen specific for the disease or disorder, wherein the polynucleotide is administered to the subject in an amount sufficient to modulate the immune response induced in the subject by the antigen.

225. The method of claim 223, wherein the polynucleotide further comprises a nucleotide sequence encoding for an antigen.

226. The method of claim 223, wherein the polynucleotide further comprises at least one additional nucleotide sequence encoding a cytokine, adjuvant, co-stimulatory molecule, or at least one additional nucleotide sequence comprising a promoter.

227. The method of claim 223, wherein the subject is a mammal.

228. The method of claim 227, wherein the mammal is a human.

229. The method of claim 223, wherein said polynucleotide comprises a vector.

263. An isolated or recombinant nucleic acid comprising a nucleotide sequence selected from the group of:

(a) a nucleotide sequence that encodes an extracellular domain (ECD), said nucleotide sequence comprising an ECD coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding an ECD, said ECD comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof; and

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding

affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 and/or an ability to induce a T cell proliferation response equal to or greater than that induced by human B7-1.

264. The isolated or recombinant nucleic acid of claim 263, wherein the nucleotide sequence of (c) hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) and encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

265. The isolated or recombinant nucleic acid of claim 264, further comprising at least a second nucleotide sequence that encodes a signal peptide, wherein said second nucleotide sequence is selected from the group of:

(a) a nucleotide sequence comprising a signal peptide coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a signal peptide, said signal peptide comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence encoding a signal peptide of a B7-1 polypeptide.

266. The isolated or recombinant nucleic acid of claim 265, wherein the nucleotide sequence of (c) hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) and encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or an ability to induce a T cell proliferation response about equal to or greater than that induced by human B7-1.

267. The isolated or recombinant nucleic acid of claim 265, further comprising at least a third nucleotide sequence encoding a transmembrane domain selected from the group of:

(a) a nucleotide sequence comprising a transmembrane domain coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a transmembrane domain, said transmembrane domain comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence that encodes a transmembrane domain of a B7-1 polypeptide.

268. The isolated or recombinant nucleic acid of claim 267, further comprising at least a fourth nucleotide sequence encoding a cytoplasmic domain selected from the group of:

(a) a nucleotide sequence comprising a cytoplasmic domain coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a cytoplasmic domain, said cytoplasmic domain comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence that encodes a cytoplasmic domain of a B7-1 polypeptide.

316. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has an CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

317. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide comprises a soluble polypeptide having an ability in the presence of a population of activated T cells to induce a T cell proliferation response that is less than the T cell proliferation response induced by a soluble human B7-1 polypeptide in the presence of a population of activated T cells.

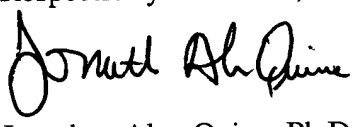
Conclusion

In view of the foregoing, Applicants believe that all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3509.

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P.O. BOX 458
Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877

Respectfully submitted,



Jonathan Alan Quine, Ph.D., J.D.
Reg. No: 41,261

Courtesy Copy of Pending Claims

43. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:1-21 and 95-142, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b); and

(d) a polynucleotide sequence comprising all or a nucleotide fragment of (a), (b), or (c), wherein the nucleotide fragment encodes a polypeptide having a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or a polypeptide having an ability to induce a T cell proliferation response that is about equal to or greater than that induced by human B7-1.

44. An isolated or recombinant nucleic acid comprising a polynucleotide sequence encoding a polypeptide, wherein the encoded polypeptide comprises an amino acid sequence which is substantially identical over at least about 150 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293 and is a non naturally-occurring amino acid sequence.

45. The nucleic acid of claim 44, wherein the encoded polypeptide is substantially identical over at least about 175 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

46. An isolated or recombinant nucleic acid comprising a nucleotide sequence coding for a polypeptide comprising the amino acid sequence set forth in any of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a subsequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide,

the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide, and wherein the amino acid sequence or subsequence is a non naturally-occurring sequence.

47. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or an ability to induce a T cell proliferation response equal to or greater than that of human B7-1.

48. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

49. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide has a decreased or a lowered binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

50. The nucleic acid of claim 43, 44, 46, or 49, wherein the encoded polypeptide induces T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

51. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

52. The nucleic acid of claim 43, 44, or 46, wherein the nucleic acid encodes a fusion protein comprising at least one additional amino acid sequence.

53. The nucleic acid of claim 52, wherein the at least one additional amino acid sequence comprises at least one Ig polypeptide.

54. The nucleic acid of claim 53, wherein the at least one Ig polypeptide comprises at least one human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

55. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises a signal sequence.

56. The nucleic acid of claim 43, 44, 46, or 49, wherein the encoded polypeptide comprises a precursor peptide.

57. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises an epitope tag sequence.

58. A cell comprising the nucleic acid of claim 43, 44, 46, or 49.

59. The cell of claim 58, wherein the cell expresses a polypeptide encoded by the nucleic acid.

60. A vector comprising the nucleic acid of claim 43, 44, 46, or 49.

61. The vector of claim 60, wherein the vector comprises a plasmid, a cosmid, a phage, a virus, a virus-like particle, or a fragment of a virus.

62. The vector of claim 60, wherein the vector is an expression vector.

63. The expression vector of claim 62, wherein the nucleic acid is operably linked to a promoter.

64. The expression vector of claim 62, further comprising a polynucleotide sequence encoding an antigen.

65. The expression vector of claim 64, wherein the antigen is a cancer antigen.

66. The expression vector of claim 64, wherein the nucleic acid is operably linked to first promoter and the polynucleotide sequence encoding the antigen is operably linked to a second promoter.

67. The expression vector of claim 65, wherein the cancer antigen is EpCam/KSA or a mutant or variant thereof.

68. The expression vector of claim 67, wherein the expression vector comprises the vector shown in Figure 22B.

69. A host cell comprising the vector of claim 60.

70. A composition comprising the nucleic acid of claim 43, 44, 46, or 49 and an excipient.

71. The composition of claim 70, wherein the excipient is a pharmaceutically acceptable excipient.

72. A composition of matter comprising at least one nucleic acid of claim 43, 44, 46, or 49.

73. The composition of claim 72, wherein the composition comprises a library comprising at least about 2, 5, 10, 50 or more nucleic acids.

223. A method of modulating an immune response in a subject, comprising: administering to the subject a polynucleotide comprising a nucleic acid sequence of claim 43, 46, 128, 129, 132, or 170, operably linked to a promoter sequence that controls the expression of said nucleic acid sequence, said polynucleotide being present in an amount sufficient that uptake of said polynucleotide into one or more cells of the subject occurs and sufficient expression of said nucleic

acid sequence results to produce an amount of a polypeptide effective to modulate an immune response.

224. The method of claim 223, further comprising administering to the subject an antigen specific for the disease or disorder, wherein the polynucleotide is administered to the subject in an amount sufficient to modulate the immune response induced in the subject by the antigen.

225. The method of claim 223, wherein the polynucleotide further comprises a nucleotide sequence encoding for an antigen.

226. The method of claim 223, wherein the polynucleotide further comprises at least one additional nucleotide sequence encoding a cytokine, adjuvant, co-stimulatory molecule, or at least one additional nucleotide sequence comprising a promoter.

227. The method of claim 223, wherein the subject is a mammal.

228. The method of claim 227, wherein the mammal is a human.

229. The method of claim 223, wherein said polynucleotide comprises a vector.

263. An isolated or recombinant nucleic acid comprising a nucleotide sequence selected from the group of:

(a) a nucleotide sequence that encodes an extracellular domain (ECD), said nucleotide sequence comprising an ECD coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding an ECD, said ECD comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof; and

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding

affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 and/or an ability to induce a T cell proliferation response equal to or greater than that induced by human B7-1.

264. The isolated or recombinant nucleic acid of claim 263, wherein the nucleotide sequence of (c) hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) and encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

265. The isolated or recombinant nucleic acid of claim 264, further comprising at least a second nucleotide sequence that encodes a signal peptide, wherein said second nucleotide sequence is selected from the group of:

(a) a nucleotide sequence comprising a signal peptide coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a signal peptide, said signal peptide comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence encoding a signal peptide of a B7-1 polypeptide.

266. The isolated or recombinant nucleic acid of claim 265, wherein the nucleotide sequence of (c) hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) and encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio greater than the CD28/CTLA-4 binding affinity ratio of human B7-1 or an ability to induce a T cell proliferation response about equal to or greater than that induced by human B7-1.

267. The isolated or recombinant nucleic acid of claim 265, further comprising at least a third nucleotide sequence encoding a transmembrane domain selected from the group of:

(a) a nucleotide sequence comprising a transmembrane domain coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a transmembrane domain, said transmembrane domain comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence that encodes a transmembrane domain of a B7-1 polypeptide.

268. The isolated or recombinant nucleic acid of claim 267, further comprising at least a fourth nucleotide sequence encoding a cytoplasmic domain selected from the group of:

(a) a nucleotide sequence comprising a cytoplasmic domain coding subsequence of a polynucleotide sequence selected from the group of SEQ ID NOS:1-21 and 95-142, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence encoding a cytoplasmic domain, said cytoplasmic domain comprising an amino acid subsequence of a polypeptide sequence selected from the group of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary nucleotide sequence thereof;

(c) a nucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b), wherein said nucleotide sequence encodes a polypeptide that has a CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1; and

(d) a nucleotide sequence that encodes a cytoplasmic domain of a B7-1 polypeptide.

316. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has an CD28/CTLA-4 binding affinity ratio about equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

317. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide comprises a soluble polypeptide having an ability in the presence of a population of activated T cells to induce a T cell proliferation response that is less than the T cell proliferation response induced by a soluble human B7-1 polypeptide in the presence of a population of activated T cells.